PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	01.02.2005
Applicant's or agent's file reference: SAP-715-PCT	FOR FURTHER ACTION: See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/015620	21.10.2004	21.10.2003

International Patent Classification (IPC) or both national classification and IPC

C07K14/47/ 19/00, C12N15/12, 1/21, 5/10, C12P21/02, G01N33/53, A01K67/027, A61K38/17, 48/00, A61P9/10, 17/02, 17/06, 19/02,

Applicant

Teijin Pharma Limited

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☒ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

The feature common to claims 1 to 26 is "human ChM." However, the search revealed that "human ChM" is disclosed in the document WO 01/23557 A1 (Teijin Ltd., 5 April 2001), and thus, said feature is not novel. As a result, "human ChM" makes no contribution over the prior art, and therefore, said common feature does not constitute a special technical feature. Accordingly, the inventions set forth in claims 1 to 26 can be categorized into the group of inventions described in claims 1 to 17 and 20 to 26, which have a special technical feature comprising "a polypeptide comprising the amino acid sequence represented by SEQ ID No.:9," and the group of inventions described in claims 18 and 19, which have a special technical feature comprising "a process for producing recombinant human ChM-I or recombinant human ChM1L by using a recombinant host cell capable of expressing human ChM-I or human ChM1L."

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	15-19	YES
	Claims	1-14, 20-26	NO
Inventive step (IS)	Claims		YES
	Claims	1-26	NO
Industrial applicability (IA)	Claims	1-26	YES
	Claims		NO

2. Citations and explanations:

The international search report cites the following documents:

Document 1: *Invest. Ophthalmol. Vis. Sci.*, May 2003, Vol. 44, No. 5, pages 1814-23

Document 2: WO 01/23557 A1 (Teijin Ltd.), 5 April 2001, examples, fig. 1A, 1B

Document 3: *Biochem. Biophys. Res. Commun.*, 2001, Vol. 280, No. 4, pages 1101-6

Document 4: *J. Biol. Chem.*, 1997, Vol. 272, No. 51, pages 32419-26

Document 5: *Eur. J. Biochem.*, 1999, Vol. 260, pages 869-878

Document 6: *FEBS Lett.*, 1997, Vol. 415, No. 3, pages 321-4

Document 7: *FEBS Lett.*, 1999, Vol. 458, No. 3, pages 436-40

Document 8: *Clin. Biochem.*, 1997, Vol. 30, No. 6, pages 455-63

The inventions set forth in claims 1 to 8, 10 to 14, and 20 to 26 lack novelty and do not involve an inventive step in the light of document 1.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Document 1 indicates that the C-terminal of ChM-I exhibits angiogenesis inhibitory activity, and the C-terminal of ChM-I satisfies the condition set forth in the present claims of being at least 70% homologous to the amino acid sequence represented by SEQ ID No.:9.

The inventions set forth in claims 9, 10, 12 to 14, and 26 lack novelty and do not involve an inventive step in the light of each of documents 2 and 3.

Each of documents 2 and 3 discloses the amino acid sequence for hChM1L and nucleotide sequences and the like corresponding thereto. The sequence represented by SEQ ID No.:9 and the nucleotide sequence of residues 4 to 243 of SEQ ID No.:3, described in the present claims, are included in the above sequences disclosed in documents 2 and 3.

The inventions set forth in claims 1 to 14 and 20 to 26 do not involve an inventive step in the light of a combination of either of documents 2 and 3 and documents 1 and 4 to 7.

Documents 2 and 3 compare the amino acid sequences for ChM-I and ChM1L and indicate that the two are homologous, and that Chm1L has a particularly high homology with the C-terminal portion that is extracellularly secreted after the processing of ChM-I. Documents 2 and 3 also state that ChM1L exhibits angiogenesis inhibitory activity.

Meanwhile, documents 1 and 4 to 7 state that the C-terminal portion that is extracellularly secreted after the processing of ChM-I exhibits angiogenesis inhibitory activity and bone absorption inhibitory activity.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Therefore, a person skilled in the art could easily conceive of implementing genetic engineering means to prepare the C-terminal portion of ChM1L, which documents 2 and 3 indicate has high homology with ChM-I, and could easily predict the effect of doing so.

The invention set forth in claims 15 to 17 does not involve an inventive step in the light of a combination of document 1 and document 8, or a combination of either of documents 2 and 3 and documents 1 and 4 to 8.

Document 8 discloses the use of a protein modifier and Triton X-114 as a method for removing endotoxin when preparing a recombinant protein from E. coli.

Therefore, when using a known host such as E. coli to produce a polypeptide comprising the C-terminal portion of ChM-I, disclosed in document 1, or a polypeptide comprising the C-terminal portion of ChM1L, arrived at through a combination of either of documents 2 and 3 and documents 1 and 4 to 7, a person skilled in the art could easily conceive of using the method disclosed in document 8, and could easily predict the effect of doing so.

The invention set forth in claims 18 and 19 does not involve an inventive step in the light of a combination of any of documents 1 to 3 and document 8.

When using a known host such as E. coli to produce the ChM-I disclosed in document 1 or the ChM1L disclosed in documents 2 and 3, a person skilled in the art could easily conceive of using the method disclosed in document 8, and could easily predict the effect of doing so.